New Claim 26 has been added to further bring out some characteristics of the homo- and copolymers of N-vinylpyrrolidone which are addressed on page 12, indicated lines 20 to 22, of the application.

Additionally, applicants have corrected Table 2 on page 15 of the application. As noted by the Examiner, the dissolution times indicated for the preparations exhibiting a "sustained release" erroneously indicated minutes instead of the correct unit of hours. As such, applicants merely correct an obvious error and the correction does not introduce new matter. Favorable action is respectfully solicited.

The Examiner rejected Claims 1, 2, 4, 6 to 8, 10 to 16, and 20 to 25 under 35 U.S.C. §103(a) as being unpatentable in light of the teaching of ***Andries et al.*** (US 6,197,779) when taken in view of the disclosures of ***Goertz et al.*** (US 4,801,460), of ***Nakamichi et al.*** (US 5,456,923), of ***Sasatani et al.*** (US 5,876,760), and of ***Takada*** (US 5,350,741), and further in view of the disclosure of ***Baert et al.*** (EP 0 872 233).

As concerns the teaching of ***Andries et al.*** and the disclosures of ***Goertz et al.***, ***Nakamichi et al.***, ***Sasatani et al.***, and of ***Takada*** the Examiner essentially reiterated the position taken in the earlier proceedings and applicants' respectfully refer to their respective earlier remarks in the reply dated December 13, 2005, and the submission dated May 06, 2006, both of which papers are herewith incorporated by reference.

The Examiner applied the disclosure of ***Baert et al.*** for showing the use of a combination of PVP and hydroxypropyl methyl cellulose (HPMC) as carrier for a controlled release antiviral dosage form, to further support the position that a person of ordinary skill would have been motivated to employ HPMC in a preparation

- comprising HIV inhibiting pyrimidine derivatives addressed by ***Andries et al.***;
- in form of a solid solution in a homo- or copolymer of N-vinylpyrrolidone as a carrier as addressed in the disclosure of ***Goertz et al.***;
- together with HPMC which is described by ***Nakamichi et al.*** as being equally useful as a solid carrier as homo- or copolymers of N-vinylpyrrolidone; and
- together with polyethylene glycol castor oil ester and citric which are mentioned by ***Sasatani et al.*** and by ***Takada*** as known excipients.

It is respectfully noted that ***Baert et al.*** relates to a preparation of the pharmaceutical ***Loviride***, which comprises a solid dispersion of ***Loviride*** and one or more pharmaceutically acceptable water-soluble polymers.[2] The respective pharmaceutical is structurally distinct from the compounds of the formulae (I) to (VI) referenced in applicants claims. Most notably, ***Loviride*** contains only one center of

2) Cf. page 2, indicated lines 52 to 55, of ***EP 0 872 233***.

basicity, namely a phenyl bound amino nitrogen, whereas the compounds (I) to (VI) referenced in applicants' claims contain at least one further center of basicity, namely a basic heterocycle which carries an imino nitrogen. Due to there structural distinctions, both the polarity and the basicity of the compounds (I) to (VI) can be expected to be markedly distinct from the corresponding properties of *Loviride*. Properties such as the polarity and the basicity have, however, a strong impact on the dissolution properties of a compound and, correspondingly, on the interaction of the compound with water-soluble polar polymers. A person of ordinary skill in the art can therefore not reasonably expect that means which are suitable to provide for a sustained release dosage form of *Loviride* will act in an equivalent manner when the active ingredient is replaced by a compound according to applicants' formulae (I) to (VI).

It is further respectfully urged that ***Baert et al.*** address a combination of HPMC and crospovidone rather than a combination of polyvinylpyrrolidone (PVP) and HPMC.[3] Crospovidone is, in contrast to PVP, a hydrophilic, insoluble or poorly water-soluble crosslinked polymer,[4] which acts as a disintegrant and ensures an *immediate* release of the active ingredient by rapidly disintegrating the preparation in the stomach.[5] The disintegrant properties result because the cross-linked polymer has a large coefficient of expansion which means that crospovidone particles swell upon contact with and aqueous environment and thus destroy the matrix of the solid dispersion. It is immediately apparent that disintegrants are used only, as pointed out by ***Baert et al.***, in immediate release preparations.[6]

It should also be noted that crospovidone is, due to the cross-linking, not capable of melting and, thus, not suitable as a PVP material in accordance with the teaching of ***Goertz et al.*** or as matrix material in accordance with applicants' invention.

The disclosure of ***Baert et al.*** is therefore not deemed to close or even narrow the gap between applicants' invention on the one hand, and the teaching of ***Andries et al.*** and the disclosures of ***Goertz et al.***, ***Nakamichi et al.***, ***Sasatani et al.***, and of ***Takada*** on the other hand.

The Examiner urged that the optimization of result effective parameters was deemed to be within the skill in the art. The respective argument begs the question which of the parameters are effective to achieve a particular result. To support an argument that a claimed invention is obvious under Section 103(a) a particular parameter must first be recognized as a result-effective variable, i.e., a variable which achieves a recognized result, before the determination of the optimum or workable ranges of said variable might be characterized as routine experimentation.[7] The Court's holding in *In re Boesch*, 617 F.2d 272, 205 USPQ 215 (CCPA 1980) which was cited by the Examiner is fully

3) Cf. page 6, indicated lines 3 to 5, of ***EP 0 872 233***.

4) Cf. page 6, indicated lines 3 to 5, of ***EP 0 872 233***.

5) Cf. page 5, indicated line 56, to page 6, indicated line 2, of ***EP 0 872 233***.

6) Cf. page 5, indicated lines 56 and 57, of ***EP 0 872 233***.

7) *In re Antonie*, 559 F.2d 618, 195 USPQ 6 (CCPA 1977).

consonant with those principles. In the case referenced by the Examiner the prior art suggested a proportional balancing of constituents of an alloy to achieve certain results, ie. the prior art specifically pointed out that the proportion of the constituents was result effective. It is also respectfully noted that citing references which merely indicate that the elements and/or features which are recited in a claim are separately known in the art is not a sufficient basis for concluding that the combination of the elements which is defined by the claims would have been obvious to a person of ordinary skill in the art.[8] To render the claimed combination of elements obvious it is also necessary that there be evidence of a motivating force which would impel a person skilled in the art to do what applicants have done. The mere fact that the prior art could be combined and/or modified so as to arrive at the applicant's invention as claimed does not suffice to render such a modification *prima facie* obvious unless the prior art suggests the desirability of the modification.[9] The fact that the respective combination and/or modification is within the skill in the art does not allow a conclusion that the prior art provides for a motivation to make the pertinent combination and/or modification.[10] "Would have been able to produce" does not meet the standards applicable to a determination under Section 103(a).[11]

It is therefore respectfully urged that the subject matter of applicants' claims cannot be deemed to be rendered obvious within the meaning of Section 103(a) by the teaching of ***Andries et al.*** and the disclosures of ***Goertz et al.***, ***Nakamichi et al.***, ***Sasatani et al.***, and of ***Takada*** when further taken in view of the disclosure of ***Bard et al.*** Favorable reconsideration of the Examiner's position and withdrawal of the rejection is respectfully solicited.

REQUEST FOR EXTENSION OF TIME

It is respectfully requested that a *three* month extension of time be granted in this case. The respective *$1020.00* fee is paid by credit card (Form PTO–2038 enclosed).

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8) Cf. *Ex parte Hiyamizu*, 10 USPQ2d 1393 (BPAI 1988).

9) Cf. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991); *In re Gordon*, 733 F.2d 900, 221 USPQ 1125 (Fed. Cir. 1984); see also, eg., *Interconnect. Planning Corp. v. Feil*, 774 F.2d 1132, 227 USPQ 543 (Fed. Cir. 1985); *In re Grabiak*, 769 F.2d 729, 226 USPQ 870 (Fed. Cir. 1985); *In re Sernaker*, 702 F.2d 989, 217 USPQ 1 (Fed. Cir. 1983).

10) Cf. *In re Rouffet*, 149 F.3d 1350, 47 USPQ2d 1453 (Fed. Cir. 1998); *Al Site Corp. v. VSI International, Inc.*, 174 F.3d 1308, 50 USPQ2d 1161 (Fed. Cir. 1999).

11) *Orthokinetics, Inc. v. Safety Travel Chairs, Inc.*, 806 F.2d 1565, 1 USPQ2d 1081 (Fed. Cir. 1986).

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Respectfully submitted,
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Encl.: SPECIFICATION AMENDMENTS (Appendix I)
CLAIM AMENDMENTS (Appendix II)

JR/BAS